09/830221

PATENT

1 of 2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Haynes, Joel R.
Wonderling, Ramani S.
Stinchcomb, Dan T.

U.S. Patent No.: 6,770,282 B1

Issue Date: August 3, 2004

Atty. File No.: DE-3-C2-PUS

For: 'CATIONIC LIPID-MEDIATED ENHANCEMENT OF NUCLEIC ACID IMMUNIZATION OF CATS'

REQUEST FOR CERTIFICATE OF CORRECTION OF PATENT FOR PTO MISTAKE (37 C.F.R. 1.322(a))

CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE U.S. POSTAL SERVICE AS FIRST CLASS MAIL ADDRESSED TO COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VIRGINIA 22313-1450, THIS 12TH DAY OF AUGUST 2005.

HESKA CORPORATION

By: Susan A. Gordon
Susan A. Gordon

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Certificate
AUG 17 2005
of Correction

Dear Sir:

This is a request for a Certificate of Correction under 37 C.F.R. 1.322(a). Attached in duplicate is Form PTO-1050. The error in this patent is obviously a scanning error made by the USPTO. The correction to Claim 7 is supported by the amendments to the claims submitted in the Interview Summary, filed March 3, 2004, and accepted by the Examiner in the Notice of Allowance, dated March 23, 2004 (see copies of both documents attached).

In Claim 7, column 22, line 12, please delete "wherein n single" and replace with --wherein a single--.

Respectfully submitted,

Dated: August 12, 2005

By: Richard J. Stern

Richard J. Stern, Ph.D.
Registration No. 50,668
Heska Corporation
3760 Rocky Mountain Ave.
Loveland, Colorado 80538
Telephone: (970) 493-7272
Facsimile: (970) 619-3011

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO : **6,770,282 B1**

DATED : **Aug. 3, 2004**

INVENTOR(S) : **Joel R. Haynes, Ramani S. Wonderling, Dan T. Stinchcomb**

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Claim 7, column 22, line 12, please delete "wherein n single" and replace with --wherein a single--.

MAILING ADDRESS OF SENDER: **Heska Corporation**
Intellectual Property Dept.
3760 Rocky Mountain Ave.
Loveland, Colorado 80538

PATENT NO. **6,770,282 B1**

No. of additional copies

AUG 18 2005

P15/REV02

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO : **6,770,282 B1**

DATED : **Aug. 3, 2004**

INVENTOR(S) : **Joel R. Haynes, Ramani S. Wonderling, Dan T. Stinchcomb**

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Claim 7, column 22, line 12, please delete "wherein n single" and replace with --wherein a single--.

MAILING ADDRESS OF SENDER: **Heska Corporation**
Intellectual Property Dept.
3760 Rocky Mountain Ave.
Loveland, Colorado 80538

PATENT NO. **6,770,282 B1**

No. of additional copies

AUG 1 8 2005

Auto-Reply Facsimile Transmission

TO: Fax Sender at 970+491+9976

Fax Information
Date Received: 3/3/2004 4:45:45 PM [Eastern Standard Time]
Total Pages: 5 (including cover page)

ADVISORY: This is an automatically generated return receipt confirmation of the facsimile transmission received by the Office. Please check to make sure that the number of pages listed as received in Total Pages above matches what was intended to be sent. Applicants are advised to retain this receipt in the unlikely event that proof of this facsimile transmission is necessary. Applicants are also advised to use the certificate of facsimile transmission procedures set forth in 37 CFR 1.8(a) and (b), 37 CFR 1.6(f). Trademark Applicants, also see the Trademark Manual of Examining Procedure (TMEP) section 306 et seq.

Received Cover Page =======>

MAR-03-2004 WED 02:32 PM HESKA CORPORATION FAX NO. 970+491+9976 P. 01

Facsimile

HESKA
The Science of Caring for Companion Animals

1613 Prospect Parkway
Fort Collins, CO 80525
970-493-7272 (t)
970-491-9976 (f)

Date: March 3, 2004

PLEASE DELIVER THE FOLLOWING PAGE(S) TO:

Name: Examiner Shanon A. Foley, Group Art Unit 1648

Facsimile Number: 703-872-9306

Telephone Number: 571-272-0898

Pages: 5 (including this cover page)

Subject: Attorney File No. DE-3-C2-PUS
U.S. Patent Application Serial No: 09/830,221

From: Richard J. Storm, Ph.D. (970-493-7272 - Ext 4174)

CONFIDENTIALITY NOTICE

The documents accompanying this FACSIMILE transmission may contain confidential information which is legally privileged. The information is intended only for the use of the individual or entity named above. If you are not the intended recipient, or the person responsible for delivering it to the intended recipient, you are hereby notified that any disclosure, copying, distribution or use of any of the information contained in this transmission is strictly PROHIBITED. If you have received this transmission in error, please immediately notify us by telephone and mail the original transmission to us. Thank you.

PAGE 1/5 * RCVD AT 3/3/2004 4:45:45 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/4 * DNIS:8729306 * CSID:970+491+9976 * DURATION (mm-ss):01-20

Facsimile

HESKA

The Science of Caring for Companion Animals

1613 Prospect Parkway
Fort Collins, CO 80525
970-493-7272 (t)
970-491-9976 (f)

Date: March 3, 2004

PLEASE DELIVER THE FOLLOWING PAGE(S) TO:

Name: Examiner Shanon A. Foley, Group Art Unit 1648

Facsimile Number: 703-872-9306

Telephone Number: 571-272-0898

Pages: 5 (including this cover page)

Subject: Attorney File No. DE-3-C2-PUS

U.S. Patent Application Serial No: 09/830,221

From: Richard J. Stern, Ph.D. (970-493-7272 - Ext 4174)

ATTN: MAIL STOP AF
PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:

Haynes, Joel R.
Wonderling, Ramani S.
Stinchcomb, Dan T.

Serial No.: 09/830,221

Filed: August 10, 2001

Atty. File No.: DE-3-C2-PUS

For: "CATIONIC LIPID-MEDIATED ENHANCEMENT OF NUCLEIC ACID IMMUNIZATION OF CATS"

Group Art Unit: 1648

Examiner: Foley, Shanon A.

INTERVIEW SUMMARY

CERTIFICATE OF FACSIMILE TRANSMISSION

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING FACSIMILE TRANSMITTED TO FAX NO. 703-872-9306, ADDRESSED TO MAIL STOP AF, COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450, THIS 3RD DAY OF MARCH 2004.

HESKA CORPORATION

By: Susan A. Gordon

Susan A. Gordon

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

In response to the Examiner interview of February 17, 2003, Applicants submit the following claims for consideration:

AMENDMENTS TO THE CLAIMS

1-27 (Canceled)

28. (New) A method to protect a felid from rabies infection, said method comprising parenterally administering to said felid a composition comprising a purified nucleic acid molecule encoding rabies glycoprotein G, wherein said purified nucleic acid molecule is complexed with a cationic lipid.

29. (New) The method of Claim 28, wherein said cationic lipid comprises a tetramethyltetraalkyl spermine analog lipid.

30. (New) The method of Claim 28, wherein said composition further encodes an immunomodulator.

31.(New) The method of Claim 28, wherein said felid is selected from the group consisting of domestic cats, wild cats and zoo cats.

32.(New) The method of Claim 28, wherein said felid is selected from the group consisting of domestic cats, lions, tigers, leopards, panthers, cougars, bobcats, lynx, jaguars, cheetahs and servals.

33.(New) The method of Claim 28, wherein the felid is a domestic cat.

34.(New) The method of Claim 28, wherein a single administration of said composition elicits an immune response.

35.(New) The method of Claim 28, wherein said composition enhances an immune response compared to administration of a naked DNA vaccine encoding rabies glycoprotein G

36.(New) The method of Claim 28, wherein said step of administering said composition is selected from the group consisting of intramuscular administration, intravenous administration, subcutaneous administration, intradermal administration and intraperitoneal administration.

37.(New) The method of Claim 28, wherein said step of administering effects about 75% seroconversion in a population of felids administered said purified nucleic acid molecule.

38.(New) The method of Claim 28, wherein said step of administering effects about 100% seroconversion in a population of felids administered said purified nucleic acid molecule.

39.(New) The method of Claim 28, wherein said purified nucleic acid molecule:lipid ratio is from about 1:10 to about 10:1.

40.(New) The method of Claim 28, wherein said purified nucleic acid molecule is administered in a dose of from about 75 micrograms to about 1,000 micrograms.

41.(New) The method of Claim 28, wherein said purified nucleic acid molecule is administered in a dose of not more than about 75 micrograms.

42.(New) The method of Claim 28, wherein said composition is dehydrated and subsequently rehydrated prior to administration.

43.(New) The method of Claim 28, wherein said composition further comprises an excipient.

REMARKS

Interview Summary

On February 17, 2004, Applicants representatives, Richard Stern and Theresa Brown, met with Examiner Shanon Foley and discussed pending Claims 1-27. The Examiner acknowledged the combination of Paoletti with McCluskie et al. and Ray et al. was incorrect and that Claim 3, and all claims depending from it, would be allowable.

The Examiner then stated she had identified new prior art and any further consideration of the rejected claims would be made in light of the newly identified art. She then presented Applicants representatives with copies of this newly identified art which consisted of:

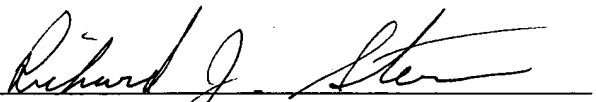
- WO 98/03660
- Yokoyama, et al, FEMS Immunology and Medical Microbiology, 1997, 14(4):221-30
- Cuisinier et al., Vaccine 1997, 15(10):1085-1094

CONCLUSION

In view of discussions held with the Examiner, Applicants believe the newly submitted claims are in condition for allowance. If there are any questions, the Examiner is encouraged to contact the undersigned.

Respectfully submitted,

Dated: March 3, 2004

By: 

Richard J. Stern, Ph.D.
Registration No. 50,668
Heska Corporation
1613 Prospect Parkway
Fort Collins, Colorado 80525
Telephone: (970) 493-7272 (ext. 4174)
Facsimile: (970) 491-9976

P. 01

TRANSACTION REPORT

MAR-03-2004 WED 02:33 PM

DATE	START	RECEIVER	TX TIME	PAGES	TYPE	NOTE	M#	DP
MAR-03	02:32 PM	17038729306	1'07"	5	SEND	OK	109	

TOTAL : 1M 7S PAGES: 5

Facsimile

HESKA

The Science of Caring for Companion Animals

1613 Prospect Parkway
Fort Collins, CO 80525
970-493-7272 (t)
970-491-9976 (f)

Date: March 3, 2004

PLEASE DELIVER THE FOLLOWING PAGE(S) TO:

Name: Examiner Shanon A. Foley, Group Art Unit 1648

Facsimile Number: 703-872-9306

Telephone Number: 571-272-0898

Pages: 5 (including this cover page)

RJS/TAB/CTV

COPY

UNITED STATES PATENT AND TRADEMARK OFFICE

OIPE
AUG 15 2005

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

'04 MAR 25 RCV'D

NOTICE OF ALLOWANCE AND FEE(S) DUE

26949 7590 03/23/2004

HESKA CORPORATION
INTELLECTUAL PROPERTY DEPT.
1613 PROSPECT PARKWAY
FORT COLLINS, CO 80525

DOCKETED

EXAMINER	
FOLEY, SHANON A	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/23/2004

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,221	08/10/2001	Joel R. Haynes	DE-3-C2-PUS	3163

TITLE OF INVENTION: CATIONIC LIPID-MEDIATED ENHANCEMENT OF NUCLEIC ACID IMMUNIZATION OF CATS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$665	$0	$665	06/23/2004

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:
A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

☐ Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 11/03) Approved for use through 04/30/2004.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,221	08/10/2001	Joel R. Haynes	DE-3-C2-PUS	3163

26949 7590 03/23/2004

HESKA CORPORATION
INTELLECTUAL PROPERTY DEPT.
1613 PROSPECT PARKWAY
FORT COLLINS, CO 80525

EXAMINER	
FOLEY, SHANON A	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/23/2004

Determination of Patent Term Extension under 35 U.S.C. 154 (b)
(application filed after June 7, 1995 but prior to May 29, 2000)

The Patent Term Extension is 0 day(s). Any patent to issue from the above-identified application will include an indication of the 0 day extension on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Extension is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (703) 305-1383. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

Notice of Allowability	Application No.	Applicant(s)	
	09/830,221	HAYNES ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *3/3/04*.

2. ☒ The allowed claim(s) is/are *28-43*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

The application has been amended as follows:

The first line of the specification has been amended to include the continuing data:

This application is a U.S. national stage application of PCT International Application No. PCT/US99/24769 and claims priority to provisional application 60/122,446, filed March 2, 1999, now abandoned, and provisional application 60/105,469 filed October 23, 1998, now abandoned.

At the interview on February 17, 2003, the following prior art was discussed of interest.

Audonnet et al. (WO 98/03660) claim a vaccine formulation for felines comprising a plasmid expressing heterologous genes, one of which is glycoprotein G from rabies, see claim 1. However, Audonnet et al. do not complex the polynucleotide vaccine formulation with a cationic lipid. Further, Audonnet et al. do not provide a working example demonstrating prophylactic efficacy in felines. The data in the working examples of the instant specification clearly shows unexpected results with the claimed formulation because cats exhibited a protective, neutralizing antibody response and mice did not. Therefore, it is evident that the asserted protective efficacy of the vaccine composition of Audonnet et al. is indeterminable because the reference does not evaluate the immune response upon administrations to cats.

Cuisinier et al. (Vaccine. July, 1997; 15 (10): 1085-1094) teach DNA vaccination with plasmids encoding structural FIV structural proteins. However, the data obtained by Cuisinier et

al. do not provide any evidence of success of administering a plasmid encoding rabies glycoprotein G, especially since Cuisinier et al. teach that cats did not develop neutralizing titers to FIV gp120, see the results and discussion sections. Further, Cuisinier et al. do not complex the plasmid with a cationic lipid.

Yokoyama et al. (FEMS. 1996; 14: 221-230) teach that DNA complexed with cationic lipids induces antibodies and CTL. However, Yokoyama et al. do not teach or suggest the effect of administering such a composition expressing rabies glycoprotein G to cats. As discussed above, the data in the working examples demonstrate unexpected neutralizing antibody titers in cats where none was observed in mice. Yokoyama et al. do not indicate that there would be a difference in immune response to a DNA complex with a cationic lipid in different hosts.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley

JAMES HOUSEL 3/22/04
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice of References Cited	Application/Control No. 09/830,221	Applicant(s)/Patent Under Reexamination HAYNES ET AL.	
	Examiner Shanon Foley	Art Unit 1648	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N	WO 98/03660	01-1998	PCT	Audonnet et al.	-----
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Cuisinier et al. Vaccine. July, 1997; 15 (10): 1085-1094.
	V	Yokoyama et al. FEMS. 1996; 14: 221-230.
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

RJS/TAB/CTV/SG DE-3-C2-PLS

US006770282B1

(12) **United States Patent**
Haynes et al.

(10) **Patent No.: US 6,770,282 B1**
(45) **Date of Patent: Aug. 3, 2004**

Proofed 9-13-04/TO

(54) **CATIONIC LIPID-MEDIATED ENHANCEMENT OF NUCLEIC ACID IMMUNIZATION OF CATS**

(75) Inventors: **Joel R. Haynes**, Mazomanie, WI (US); **Ramani S. Wonderling**, Waukegan, IL (US); **Dan T. Stinchcomb**, Fort Collins, CO (US)

(73) Assignee: **Heska Corporation**, Fort Collins, CO (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/830,221**

(22) PCT Filed: **Oct. 22, 1999**

(86) PCT No.: **PCT/US99/24769**

§ 371 (c)(1),
(2), (4) Date: **Aug. 10, 2001**

(87) PCT Pub. No.: **WO00/24428**

PCT Pub. Date: **May 4, 2000**

Related U.S. Application Data

(60) Provisional application No. 60/122,446, filed on Mar. 2, 1999, now abandoned, and provisional application No. 60/105,469, filed on Oct. 23, 1998, now abandoned.

(51) **Int. Cl.**[7] **A61K 39/39**; A61K 39/385; A61K 39/12; A61K 39/205

(52) **U.S. Cl.** **424/196.11**; 424/193.1; 424/204.1; 424/224.1

(58) **Field of Search** 424/450, 461, 424/193.1, 196.11, 197.11, 204.1, 207.1, 216.1, 221.1, 224.1, 229.1, 234.1, 265.1, 269.1, 275.1

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,726,946 A		2/1988	Bass et al.	424/89
5,505,941 A	*	4/1996	Paoletti	424/93.2
5,703,055 A		12/1997	Felgner et al.	514/44

FOREIGN PATENT DOCUMENTS

WO	WO 95/30019	11/1995
WO	WO 98/03660	* 1/1998
WO	WO 99/66879	12/1999

OTHER PUBLICATIONS

Cuisinier et al. Vaccine. Jul., 1997; 15 (10): 1085–1094.*
Yokoyama et al. FEMS. 1996; 14: 221–230.*
Ray et al. Vaccine. 1997; 15 (8): 892–895.*
McCluskie et al. Antisense and Nucleic Acid Drug Development. 1998; 8: 401–414.*
Davis et al., 1997, *Vaccine*, vol. 15, No. 8, pp. 849–852.
Donnelly et al., 1997, *Annu. Rev. Immunol.*, vol. 15, pp. 617–648.
Fynan et al., 1993, *Proc. Matl. Acad. Sci. USA*, vol. 90, pp. 11478–11482.
Gramzinski et al., 1998, *Molecular Medicine*, vol. 4, pp. 109–118.
Gregoriadis et al., 1997, *FEBS Letters*, vol. 402, pp. 107–110.
Ishii et al., 1997, *Aids Research and Human Retroviruses*, vol. 13, No. 16, pp. 1421–1428.
McCluskie et al., 1998, *Antisense & Nucleic Acid Drug Development*, vol. 8, pp. 401–414.
Norman et al., 1997, *Vaccine*, vol. 15, No. 8, pp. 801–803.
Osorio et al., 1999, *Vaccine*, vol. 17, pp. 1109–1116.
Philip et al., 1994, *Molecular and Cellular Biology*, pp. 2411–2418.
Stamatatos et al., 1988, *Biochemistry*, vol. 27, pp. 3917–3925.
Stopeck et al., 1998, *Cancer Gene Therapy*, vol. 5, No. 2, pp. 119–126.
Xiang et al., 1996, *Virology*, vol. 219, pp. 220–227.
Yokoyama et al., 1996, *FEMS Immunology and Medical Microbiology*, vol. 14, pp. 221–230.

* cited by examiner

Primary Examiner—James Housel
Assistant Examiner—Shanon Foley
(74) *Attorney, Agent, or Firm*—Heska Corporation

(57) **ABSTRACT**

The present invention relates to a method to introduce a nucleic acid molecule into a felid by administration of a nucleic acid-cationic lipid complex composition. The method includes the step of administering to the felid, by a parenteral route, a nucleic acid-cationic lipid complex to elicit and/or enhance an immune response. In one embodiment, this method enhances the immune response in a felid compared to a method in which a naked DNA vaccine is administered to a felid. Also provided is a method to deliver a nucleic acid to a felid. This method comprises parenterally administering to the felid a composition that includes a nucleic acid molecule complexed with a cationic lipid.

16 Claims, No Drawings

sectioned using a cryostat and the sections were stained using hematoxylin and eosin to analyze the population of cells infiltrating the sites of injection. Muscle samples were also stained with antibodies specific for B-cells (anti-CD79a antibodies) using techniques known to those skilled in the art.

No differences were seen among the various lymph nodes with respect to cell infiltration. In the muscle samples where vehicle alone, lipid alone or naked rabies G vector was injected, the infiltrating population of cells were mostly macrophage-like cells. In contrast, in the muscle sample where the formulation comprising rabies G vector complexed with lipid was infected, the infiltrating cells were predominantly lymphocyte-like cells. Staining results with anti-CD79a antibodies suggested that the majority of lymphocytes present were T cells.

These results, as well as others provided herein, suggest that administration of nucleic acid molecules complexed with cationic lipids to cats leads to enhanced expression of the protein encoded by the nucleic acid molecule and infiltration of lymphocytes to the injection site which apparently does not occur when naked nucleic acid molecules are administered in a similar manner. Without being bound by theory, it is believed that this infiltration of lymphocytes might explain the enhanced immune response seen with nucleic acid molecule-cationic lipid complexes of the present invention.

While various embodiments of the present invention have been described in detail, it is apparent that modifications and adaptations of those embodiments will occur to those skilled in the art. It is to be expressly understood, however, that such modifications and adaptations are within the scope of the present invention, as set forth in the following claims.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 2

<210> SEQ ID NO 1
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Primer

<400> SEQUENCE: 1

ttcccaacta taccactatc tcgtcta 27

<210> SEQ ID NO 2
<211> LENGTH: 28
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic Primer

<400> SEQUENCE: 2

ctagaagcca cagctgccct ccacagag 28

What is claimed is:

1. A method to protect a felid from rabies infection, said method comprising parenterally administering to said felid a composition comprising a purified nucleic acid molecule encoding rabies glycoprotein G, wherein said purified nucleic acid molecule is complexed with a cationic lipid.

2. The method of claim 1, wherein said cationic lipid comprises a tetramethyltetraalkyl spermine analog lipid.

3. The method of claim 1, wherein said composition further encodes an immunomodulator.

4. The method of claim 1, wherein said felid is selected from the group consisting of domestic cats, wild cats and zoo cats.

5. The method of claim 1, wherein said felid is selected from the group consisting of domestic cats, lions, tigers, leopards, panthers, cougars, bobcats, lynx, jaguars, cheetahs and servals.

6. The method of claim 1, wherein the felid is a domestic cat.

7. The method of claim 1, wherein a single administration of said composition elicits an immune response.

8. The method of claim 1, wherein said composition enhances an immune response compared to administration of a naked DNA vaccine encoding rabies glycoprotein G.

9. The method of claim 1, wherein said step of administering said composition is selected from the group consisting of intramuscular administration, intravenous administration, subentaneous administration, intradermal administration and intraperitoneal administration.

10. The method of claim 1, wherein said step of administering effects about 75% seroconversion in a population of felids administered said purified nucleic acid molecule.

11. The method of claim 1, wherein said step of administering effects about 100% seroconversion in a population of felids administered said purified nucleic acid molecule.

12. The method of claim 1, wherein said purified nucleic acid molecule:lipid ratio is from about 1:10 to about 10:1.

13. The method of claim 1, wherein said purified nucleic acid molecule is administered in a dose about 75 micrograms to about 1,000 micrograms.

14. The method of claim 1, wherein said purified nucleic acid molecule is administered in a dose of not more than about 75 micrograms.

15. The method of claim 1, wherein said composition is dehydrated and subsequently rehydrated prior to administration.

16. The method of claim 1, wherein said composition further comprises an excipient.

* * * * *